ROCKY MOUNTAIN SPOTTED FEVER

✓DISEASE AND EPIDEMIOLOGY

Clinical Description:

The onset of Rocky Mountain Spotted Fever (RMSF) is sudden. Cases usually present with a moderate to high fever, significant malaise, muscle pain, headache, chills, and eye inflammation. Over half of cases develop a rash or small bruises on the arms and legs, which typically begins 2–6 days after the onset of illness. The rash spreads to much of the body, including the palms and soles. Among untreated individuals, these signs and symptoms typically persist for 2–3 weeks, and the case-fatality rate ranges from 13–25%. More advanced manifestations include loss of red blood cells (anemia) and platelets (thrombocytopenia), severe clotting disorders, damage to the major organ systems, and shock. If the disease is promptly recognized and treated, death is uncommon. However, overall in the U.S., the reported case fatality rate for RMSF has been 3–5% in recent years.

Causative Agent:

Rocky Mountain spotted fever is caused by the bacterium *Rickettsia rickettsii*.

Differential Diagnosis:

Differential diagnosis for RMSF includes ehrilichiosis, meningococcemia and enteroviral infection.

Laboratory identification:

Serologic assays are the most widely available and frequently used methods for confirming cases of Rocky Mountain spotted fever. Blood samples taken early (acute) and late (convalescent) in the disease are the preferred specimens for evaluation. Most patients demonstrate increased IgM titers by the end of the first week of illness. Diagnostic levels of IgG antibody generally do not appear until 7-10 days after the onset of illness.

The most rapid and specific diagnostic assays for Rocky Mountain spotted fever rely on molecular methods like PCR which can detect DNA present in 5-10 rickettsiae in a sample. While organisms can be detected in whole blood samples obtained at the acute onset of illness in a few hours, rickettsial DNA is most readily detected in fresh skin biopsies like those used in immunostaining procedures. PCR availability is extremely limited in Utah.

> **UPHL:** UPHL can assist with RMSF diagnosis by facilitating isolation of *R. rickettsii* from clinical samples like whole blood and biopsies. These materials will be shipped unfrozen or frozen and on dry ice to ensure optimal chances of isolation at the CDC. Isolation may require several weeks, but isolates are very important for investigating differences in the pathogenic properties and antimicrobial resistance of rickettsiae which cause disease in different parts of the United States. The CDC also has the capability of performing immunostaining on biopsied tissues.

Treatment:
Treatment decisions should be based on epidemiologic and clinical clues, and should never be delayed while waiting for confirmation by laboratory results. Doxycycline, tetracycline, and chloramphenicol are the preferred antibiotics for treatment.

Case fatality:
If the disease is promptly recognized and treated, death is uncommon. However, overall in the U.S., the reported case fatality rate for RMSF has been 3–5% in recent years.

Reservoir:
The primary vector for RMSF is the dog tick (*Dermacentor variabilis*), which also serves as a reservoir. Among ticks, *R. rickettsii* is spread transovarially (adult tick to egg) and transstadially (between life stages). While several small wild animals, as well as dogs, may have antibodies to *R. rickettsii,* their role as possible reservoirs in the maintenance of RMSF is uncertain.

Transmission:
RMSF is acquired from the bite of an infected tick. Laboratory data suggest that the tick must remain attached for at least 4–6 hours before the transmission of *R. rickettsii* can occur.

Susceptibility:
Susceptibility is general. One attack probably confers lasting immunity.

Incubation period:
Signs of RMSF typically develop 1 week after exposure (range 3–14 days). The length of the incubation period is associated with the magnitude of exposure to *R. rickettsii* (more exposure, shorter incubation period).

Period of communicability:
RMSF is not communicable from person to person.

Epidemiology:
RMSF is widespread in the U.S., with most cases reported from the southern and midwestern states. RMSF is relatively rare in Utah, with cases occurring most frequently in states south of Utah. RMSF incidence rises between April and October, when the risk of contact with ticks is greatest. The risk of mortality from RMSF is higher for men, people over the age of 40, non-whites, individuals who do not develop (or recognize) the typical rash, and individuals with no reported history of a tick bite. As children tend to have more contact with tick-infested areas, most reported cases are in people under the age of 15 years. While rare, accidental transmission in the laboratory setting has been reported.

Utah averages 1 case in 5 years. The case definition requires the presence of both acute and convalescent serologies, and few clinicians order and/or patients provide convalescent sera. Therefore, it is likely that this disease is more prevalent in Utah than the data suggest.

✓PUBLIC HEALTH CONTROL MEASURES

Public health responsibility:

- Identify the source of infection and prevent further transmission.
- Investigate all suspect cases of disease and fill out and submit appropriate disease investigation forms.
- Provide education to the general public, clinicians, and first responders regarding disease transmission and prevention.
- Identify clusters or outbreaks of this disease.

Prevention:

Managing Special Situations: Response to a Tick Bite

The longer a tick remains attached to someone, the higher the likelihood of disease transmission. Individuals should promptly remove any attached tick using fine-point tweezers. The tick should not be squeezed or twisted, but grasped close to the skin and pulled straight out using steady pressure. Whenever an attached tick is removed from the body, one should monitor one's health for the appearance of rash, fever, or flu-like symptoms, and should immediately seek the advice of a health care provider should any symptoms occur, especially if the tick was attached for more than 24 hours. It may be helpful to save the tick after removal for two reasons: 1) if the person who was bitten goes on to develop signs or symptoms such as fever, flu-like symptoms, or a rash, it may be helpful for the physician to know the type of tick; and 2) depending on the circumstances of the bite (i.e., when a person was bitten, the type of tick, how long it was attached), a physician may choose to treat the person who was bitten. The tick may be kept either securely sealed in a small plastic bag or attached, with clear tape, to a piece of paper. For individuals who do not wish to keep the tick, it can be either drowned in alcohol or flushed down the toilet.

If an individual chooses to have the tick tested, the following information should be taken into account:

- Tests performed on the ticks are not perfect, and they do not test for all infections that ticks may carry. Therefore, even with a negative result, people should still monitor for the appearance of rash, fever, or other unusual symptoms and should immediately seek the advice of a health care provider should any symptoms occur.
- If someone has been infected by a tick bite, symptoms may begin to occur even before the results of tick testing are available. People should not wait for tick testing results before seeking medical advice, should any symptoms develop.
- A positive test on a tick is not an automatic indication that treatment is needed. A positive test indicates that the tick was infected but not that the tick was

successful in spreading the infection to the person bitten. The longer a tick is attached, the greater the chance that it will spread infection. Positive test results should be discussed with a health care provider.

Preventive Measures

Environmental Measures

Prevention of RMSF, along with other diseases spread by ticks, involves making the yard less attractive to ticks.

- Keep grass cut short.
- Remove leaf litter and brush from around the yard.
- Prune low lying bushes to let in more sunlight.
- Keep woodpiles and bird feeders off the ground and away from the home.
- Keep the plants around stone walls cut short.
- Use a three-foot wide woodchip, mulch, or gravel barrier where the lawn meets the woods, and remind children not to cross that barrier.
- Ask a landscaper or local nursery about plants to use in the yard that do not attract deer.
- Use deer fencing (for yards 15 acres or more).

If an individual chooses to use a pesticide to reduce the number of ticks on his/her property, he/she should be advised to hire a licensed applicator who is experienced with tick control. A local landscaper or arborist may be a licensed applicator. In general, good tick control can be achieved with no more than two pesticide applications in any year. Advise individuals to ask, when selecting an applicator, if they will provide:

- A written pest control plan that includes information on the pesticide to be used.
- Information about non-chemical pest control alternatives.
- Signs to be posted around the property after the application.

Personal Preventive Measures/Education

There is no vaccine to protect against RMSF. If someone lives, works, or spends leisure time in an area likely to have dog ticks, they should be advised of the following:

- The single most important thing to prevent a tick-borne disease is to check for ticks once a day. Favorite places ticks like to go on the body include areas between the toes, back of the knees, groin, armpits, neck, along the hairline, and behind the ears. Remember to also check children and pets. Promptly remove any attached tick using fine-point tweezers. The tick should not be squeezed or twisted, but grasped close to the skin and pulled straight out using steady pressure.
- Stick to main pathways and the centers of trails when hiking.
- Wear long-sleeved, light colored shirts and long pants tucked into socks.
- Talk to a veterinarian about the best ways to protect pets and livestock from ticks.
- Use repellents containing DEET (N,N-diethyl-m-toluamide), and choose a product that will provide sufficient protection for the amount of time spent outdoors. Product labels often indicate the length of time that one can expect

protection from a product. DEET is considered safe when used according to the manufacturer's directions. The efficacy of DEET levels off at a concentration of 30%, which is the highest concentration recommended for children and adults. DEET products should not be used on children less than two months of age. Mosquito netting may be used to cover infant carriers or to protect other areas for children less than two months of age.

The following precautions should be observed when using DEET products:

- Avoid using DEET products that combine the repellent with a sunscreen. Sunscreens may need to be reapplied too often, resulting in an over application of DEET.
- Apply DEET on exposed skin, using only as much as needed.
- Do not use DEET on the hands of young children, and avoid applying repellent to areas around the eyes and mouth.
- Do not use DEET over cuts, wounds, or irritated skin.
- Wash treated skin with soap and water after returning indoors, and wash treated clothing.
- Avoid spraying DEET products in enclosed areas.

Permethrin-containing products will kill mosquitoes and ticks on contact. Permethrin products are not designed to be applied to the skin. Clothing should be treated and allowed to dry in a well-ventilated area prior to wearing. Because permethrin binds very tightly to fabrics, once the fabric is dry, very little of the permethrin gets onto the skin.

Chemoprophylaxis:
None

Vaccine:
None

Isolation and quarantine requirements:
None

✓CASE INVESTIGATION

Reporting:
- Report all suspect and confirmed cases of RMSF.

Case Definition:

Rocky Mountain Spotted Fever (2007):

Clinical presentation

Rocky Mountain spotted fever (RMSF) is an illness caused by *Rickettsia rickettsii*, a bacterial pathogen transmitted to humans through contact with ticks. *Dermacentor* species of ticks are most commonly associated with infection, including *Dermacentor variabilis* (the American dog tick) and

Dermacentor andersoni (the Rocky Mountain wood tick), and more recently *Rhiphicephalus sanguineus* (the brown dog tick). Disease onset averages one week following a tick bite. Age specific illness is highest for children and older adults. Illness is characterized by acute onset of fever, and may be accompanied by headache, malaise, myalgia, nausea/vomiting, or neurologic signs; a macular or maculopapular rash appears 4-7 days following onset in many (~80%) patients, often present on the palms and soles. RMSF may be fatal in as many as 20% of untreated cases, and severe fulminant disease can occur. Acute illness is best detected by polymerase chain reaction (PCR) and immunohistochemical methods (IHC) in skin biopsy specimens, and occasionally by PCR in appropriate whole blood specimens taken during the 1st week of illness, prior to antibiotic treatment. Serology can also be employed for detection, however an antibody response may not be detectable in initial samples, and paired acute and convalescent samples are essential for confirmation.

Clinical evidence

Any reported fever and one or more of the following: rash, headache, myalgia, anemia, thrombocytopenia, or any hepatic transaminase elevation.

Laboratory evidence

For the purposes of surveillance,

Laboratory confirmed:

- Serological evidence of a fourfold change in immunoglobulin G (IgG)-specific antibody titer reactive with *Rickettsia rickettsii* antigen by indirect immunofluorescence assay (IFA) between paired serum specimens (one taken in the first week of illness and a second 2-4 weeks later), **or**
- Detection of *R. rickettsii* DNA in a clinical specimen via amplification of a specific target by PCR assay, **or**
- Demonstration of spotted fever group antigen in a biopsy/autopsy specimen by IHC, **or**
- Isolation of *R. rickettsii* from a clinical specimen in cell culture.

Laboratory supportive:

- Has serologic evidence of elevated IgG or IgM antibody reactive with *R. rickettsii* antigen by IFA, enzyme-linked immunosorbent assay (ELISA), dot-ELISA, or latex agglutination.

Note: Current commercially available ELISA tests are not quantitative, cannot be used to evaluate changes in antibody titer, and hence are not useful for serological confirmation. IgM tests are not strongly supported for use in serodiagnosis of acute disease, as the response may not be specific for the agent (resulting in false positives) and the IgM response may be persistent. Complement fixation (CF) tests and other older test methods are neither readily available nor commonly used.

CDC uses in-house IFA IgG testing (cutoff of ≥64), preferring simultaneous testing of paired specimens, and does not use IgM results for routine diagnostic testing.

Exposure

Exposure is defined as having been in potential tick habitats within the past 14 days before onset of symptoms. A history of a tick bite is not required.

Case classification

Confirmed: A clinically compatible case (meets clinical evidence criteria) that is laboratory confirmed.

Probable: A clinically compatible case (meets clinical evidence criteria) that has supportive laboratory results.

Suspect: A case with laboratory evidence of past or present infection but no clinical information available (e.g., a laboratory report).

Case Investigation Process:

- Fill out morbidity form
- Verify case status.
- Fill out disease investigation form.
- Determine whether patient had travel/exposure history consistent with acquisition of disease in Utah or elsewhere.
- If patient acquired disease in Utah, identify the source of transmission and eliminate it.

Outbreaks:

More then one laboratory confirmed case of RMSF in Utah in a year would constitute an outbreak.

Identification of case contacts:

None

Case contact management:

None

✓REFERENCES

Centers for Disease Control, Case Definitions for Infectious Conditions Under Public Health Surveillance. MMWR 46 (RR-10), 1997.l

Control of Communicable Diseases Manual (18th Edition), Heymann, D.L., Ed; 2004.

Red Book: 2003 Report of the Committee on Infectious Diseases (26th Edition), Larry K. Pickering MD, Ed; 2003.

Massachusetts Department of Health RMSF Disease Plan

Centers for Disease Control, RMSF site.